# CENTER FOR DRUG EVALUATION AND RESEARCH

*APPLICATION NUMBER:*

**75-179**

## CHEMISTRY REVIEW(S)

# Office of Generic Drugs

## Chemistry, Manufacturing and Controls Review

1. **CHEMIST'S REVIEW NO**: No. 7 **[Nabumetone Tablets]**

2. **ANDA**: 75-179

3. **NAME AND ADDRESS OF APPLICANT**:
Copley Pharmaceutical, Inc.
Attention: Vincent Andolina, RAC (Director, Regulatory Affairs)
25 John Road, Canton, MA 02021

4. **LEGAL BASIS for ANDA SUBMISSION**: See CR #1

5. **SUPPLEMENT(s)**: N/A

6. **PROPRIETARY NAME**: N/A

7. **NONPROPRIETARY NAME**: Nabumetone Tablets, 500 mg and 750 mg

8. **SUPPLEMENT(s) PROVIDE(s) FOR**: N/A

9. **AMENDMENTS AND OTHER DATES**: * denotes documents under current review

**Copley**:

| | |
|---|---|
| 08/04/97 | Submission of ANDA (received on 08/05/97) |
| 10/02/97 | Amendment (Re: Paragraph IV certification) |
| 10/24/97 | Amendment (addition of 500 mg tablet strength) |
| 03/02/98 | Response to NA (MAJOR) of 01/12/98 (from CR#1) |
| 03/05/98 | Response to Bioequivalence deficiencies |
| 07/16/98 | Bio amendments (two letters with the same date) |
| 07/20/98 | Bio amendment |
| 09/18/98 | Response to NA MINOR of 08/04/98 (from CR#2) |
| 04/22/99 | Response to NA MINOR of 11/03/98 (from CR#3) |
| 08/02/99 | Response to NA MINOR of 05/24/99 (from CR#4) |
| 08/06/99 | Amendment to the 08/02/99 letter |
| 08/27/99 | Telephone amendment (Re: active ingredient specs) |
| 09/22/99 | Telephone amendment (Re: stability commitment) |
| 11/24/99 | Question by Fax (Re: DMF) |
| 02/09/00 | Patent amendment |
| 02/23/00 | Patent amendment |
| 02/29/00 | Minor amendment (requesting tentative approval) |
| 04/06/00 | *Minor amendment (response to NA letter of 03/27/00) |
| 05/01/00 | *Amendment (Re: labelin FPL) |

**FDA**:

| | |
|---|---|
| 09/05/97 | Ackowledgment letter |
| 01/12/98 | NA (MAJOR) (based on CR #1, and labeling review) |
| 02/05/98 | Bio deficiency Fax (based on bio review of 01/30/98) |
| 07/27/98 | Bio letter (based on Bio review dated 07/21/98) |
| 08/04/98 | NA (MINOR) (based on CR #2 by S. Liu, Ph.D.) |
| 11/03/98 | NA (MINOR) (based on CR #3 by S. Liu, Ph.D.) |
| 05/24/99 | NA (MINOR) (based on CR #4 by S. Liu, Ph.D.) |
| 08/20/99 | Telephone amendment request (Gill, Yu vs. V. Andoliano) |
| 09/22/99 | Telephone amendment request |
| 09/28/99 | NA letter (MINOR) (based on CR #5 by S. Liu, Ph.D.) |
| 03/27/00 | NA letter (MINOR) (based on CR #6 by S. Liu, Ph.D.) |

10. **PHARMACOLOGICAL CATEGORY**: Anti-inflammatory

11. **HOW DISPENSED**: Rx

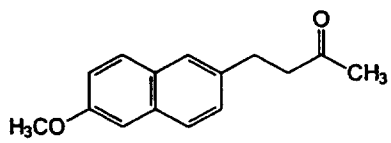
12. **RELATED IND/NDA/DMF(s)**: See CR #2

13. **DOSAGE FORM**: Oral Tablets

14. **Strength**: 500 mg and 750 mg

15. **CHEMICAL NAMES AND STRUCTURE**:

Generic name: Nabumetone
Chemical name: 2-Butanone, 4-(6-methoxy-2 naphthalenyl)-
Formula: $C_{15}H_{16}O$
Molecular weight: 228.29
CAS registry number(s): 42924-53-8
Chemical structure:




16. **RECORDS AND REPORTS**: N/A

17. **COMMENTS**:

A NA MINOR letter was issued after the last chemistry review (CR#6) because the Type II DMF was deficient. The DMF holder responded to the deficiencies in their amendment dated 04/04/00. The amendment was reviewed and was found satisfactory. As such, all CMC issues of the ANDA are resolved.

Both the bulk drug substance and the drug product do not have USP monographs.

Division of Bioequivalence has completed the review of Copley's bio amendments. DOB's comments were faxed to Copley on 07/27/98.

Labeling approval summary was signed off on 05/05/00.

Method validation request was issued on 10/07/98. Northeast Regional Laboratory sent the report (dated 12/03/98), which concluded that Copley's method appears to be suitable for regulatory analysis.

Acceptable EER dated 02/04/00.

18. **CONCLUSIONS AND RECOMMENDATIONS**:

Approvable

19. **REVIEWER**: Shing H. Liu, Ph.D.

**DATE COMPLETED**: 04/14/00
Revised on 05/09/00 (Re:labeling FPL)

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chem Rev 7

4/14/00

# Office of Generic Drugs

## Chemistry, Manufacturing and Controls Review

1. **CHEMIST'S REVIEW NO**: No. 6 **[Nabumetone Tablets]**

2. **ANDA**: 75-179

3. **NAME AND ADDRESS OF APPLICANT**:
Copley Pharmaceutical, Inc.
Attention: Vincent Andolina, RAC (Director, Regulatory Affairs)
25 John Road, Canton, MA 02021

4. **LEGAL BASIS for ANDA SUBMISSION**: See CR #1

5. **SUPPLEMENT(s)**: N/A

6. **PROPRIETARY NAME**: N/A

7. **NONPROPRIETARY NAME**: Nabumetone Tablets, 500 mg and 750 mg

8. **SUPPLEMENT(s) PROVIDE(s) FOR**: N/A

9. **AMENDMENTS AND OTHER DATES**:
* denotes documents under current review

Copley:

| | |
|---|---|
| 08/04/97 | Submission of ANDA (received on 08/05/97) |
| 10/02/97 | Amendment (Re: Paragraph IV certification) |
| 10/24/97 | Amendment (addition of 500 mg tablet strength) |
| 03/02/98 | Response to NA (MAJOR) of 01/12/98 (from CR#1) |
| 03/05/98 | Response to Bioequivalence deficiencies |
| 07/16/98 | Bio amendments (two letters with the same date) |
| 07/20/98 | Bio amendment |
| 09/18/98 | Response to NA MINOR of 08/04/98 (from CR#2) |
| 04/22/99 | Response to NA MINOR of 11/03/98 (from CR#3) |
| 08/02/99 | Response to NA MINOR of 05/24/99 (from CR#4) |
| 08/06/99 | Amendment to the 08/02/99 letter |
| 08/27/99 | Telephone amendment (Re: active ingredient specs) |
| 09/22/99 | Telephone amendment (Re: stability commitment) |
| 11/24/99 | *Question by Fax (Re: DMF) |
| 02/09/00 | *Patent amendment |
| 02/23/00 | *Patent amendment |
| 02/29/00 | *Minor amendment (requesting tentative approval) |

FDA:

| | |
|---|---|
| 09/05/97 | Ackowledgment letter |
| 01/12/98 | NA (MAJOR) (based on CR #1, and labeling review) |
| 02/05/98 | Bio deficiency Fax (based on bio review of 01/30/98) |
| 07/27/98 | Bio letter (based on Bio review dated 07/21/98) |
| 08/04/98 | NA (MINOR) (based on CR #2 by S. Liu, Ph.D.) |
| 11/03/98 | NA (MINOR) (based on CR #3 by S. Liu, Ph.D.) |
| 05/24/99 | NA (MINOR) (based on CR #4 by S. Liu, Ph.D.) |
| 08/20/99 | Telephone amendment request (Gill, Yu vs. V. Andoliano) |
| 09/22/99 | Telephone amendment request |
| 09/28/99 | NA letter (MINOR) (based on CR #5 by S. Liu, Ph.D.) |

10. **PHARMACOLOGICAL CATEGORY**: Anti-inflammatory

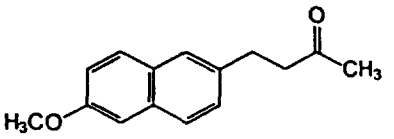
11. **HOW DISPENSED**: Rx

12. **RELATED IND/NDA/DMF(s)**: See CR #2

13. **DOSAGE FORM**: Oral Tablets

14. **Strength**: 500 mg and 750 mg

15. **CHEMICAL NAMES AND STRUCTURE**:
Generic name: Nabumetone
Chemical name: 2-Butanone, 4-(6-methoxy-2 naphthalenyl)-
Formula: $C_{15}H_{16}O$
Molecular weight: 228.29
CAS registry number(s): 42924-53-8
Chemical structure:




16. **RECORDS AND REPORTS**: N/A

17. **COMMENTS**:

CMC and DMF were found satisfactory in review #5. A NA MINOR letter was issued because of a withhold recommendation from the Office of Compliance. Now, the cGMP issues have been resolved but the DMF holder submitted an amendment in the meantime. Based on the review of this amendment, the DMF is currently inadequate.

The purpose of the minor amendment is to request a tentative approvable because Copley thought that an acceptable EER is now in order.

Both the bulk drug substance and the drug product do not have USP monographs.

Division of Bioequivalence has completed the review of Copley's bio amendments. DOB's comments were faxed to Copley on 07/27/98.

The of DMF of the drug substance has been reviewed in connection with this amendment, and was found deficient. An deficiency letter is being issued to the DMF holder.

Labeling approval summary was signed off on 03/11/98.

Method validation request was issued on 10/07/98. Northeast Regional Laboratory sent the report (dated 12/03/98), which concluded that Copley's method appears to be suitable for regulatory analysis.

Acceptable EER dated 02/04/00.

18. **CONCLUSIONS AND RECOMMENDATIONS**:
Not Approvable (MINOR Amendment)

19. **REVIEWER**: Shing H. Liu, Ph.D. **DATE COMPLETED**: 03/14/99

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Chem Rev 96

3/14/99

# Office of Generic Drugs

## Chemistry, Manufacturing and Controls Review

1. **CHEMIST'S REVIEW NO**: No. 5 **[Nabumetone Tablets]**

2. **ANDA**: 75-179

3. **NAME AND ADDRESS OF APPLICANT**:
Copley Pharmaceutical, Inc.
Attention: I. Nudelman, RAC (Director, Regulatory Affairs)
25 John Road, Canton, MA 02021

4. **LEGAL BASIS for ANDA SUBMISSION**: See CR #1

5. **SUPPLEMENT(s)**: N/A

6. **PROPRIETARY NAME**: N/A

7. **NONPROPRIETARY NAME**: Nabumetone Tablets, 500 mg and 750 mg

8. **SUPPLEMENT(s) PROVIDE(s) FOR**: N/A

9. **AMENDMENTS AND OTHER DATES**:
* denotes documents under current review

Copley:

| | |
|---|---|
| 08/04/97 | Submission of ANDA (received on 08/05/97) |
| 10/02/97 | Amendment (Re: Paragraph IV certification) |
| 10/24/97 | Amendment (addition of 500 mg tablet strength) |
| 03/02/98 | Response to NA (MAJOR) of 01/12/98 (from CR#1) |
| 03/05/98 | Response to Bioequivalence deficiencies |
| 07/16/98 | Bio amendments (two letters with the same date) |
| 07/20/98 | Bio amendment |
| 09/18/98 | Response to NA MINOR of 08/04/98 (from CR#2) |
| 04/22/99 | Response to NA MINOR of 11/03/98 (from CR#3) |
| 08/02/99 | *Response to NA MINOR of 05/24/99 (from CR#4) |
| 08/06/99 | *Amendment to the 08/02/99 letter |
| 08/27/99 | *Telephone amendment (Re: active ingredient specs) |
| 09/22/99 | *Telephone amendment (Re: stability commitment) |

FDA:

| | |
|---|---|
| 09/05/97 | Ackowledgment letter |
| 01/12/98 | NA (MAJOR) (based on CR #1, and labeling review) |
| 02/05/98 | Bio deficiency Fax (based on bio review of 01/30/98) |
| 07/27/98 | Bio letter (based on Bio review dated 07/21/98) |
| 08/04/98 | NA (MINOR) (based on CR #2 by S. Liu, Ph.D.) |
| 11/03/98 | NA (MINOR) (based on CR #3 by S. Liu, Ph.D.) |
| 05/24/99 | NA (MINOR) (based on CR #4 by S. Liu, Ph.D.) |
| 08/20/99 | Telephone amendment request (Gill, Yu vs. V. Andoliano) |
| 09/22/99 | Telephone amendment request |

10. **PHARMACOLOGICAL CATEGORY**: Anti-inflammatory

11. **HOW DISPENSED**: Rx

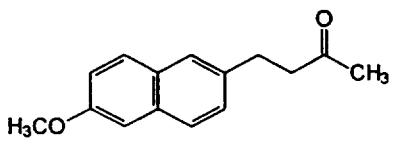
12. **RELATED IND/NDA/DMF(s)**: See CR #2

13. **DOSAGE FORM**: Oral Tablets

14. **Strength**: 500 mg and 750 mg

15. **CHEMICAL NAMES AND STRUCTURE**:

Generic name: Nabumetone
Chemical name: 2-Butanone, 4-(6-methoxy-2 naphthalenyl)-
Formula: $C_{15}H_{16}O$
Molecular weight: 228.29
CAS registry number(s): 42924-53-8
Chemical structure:




16. **RECORDS AND REPORTS**: N/A

17. **COMMENTS**:

Both the bulk drug substance and the drug product do not have USP monographs.

Division of Bioequivalence has completed the review of Copley's bio amendments. DOB's comments was faxed to Copley on 07/27/98.

The [redacted] DMF of the drug substance has been reviewed in connection with this amendment, and was found adequate.

Labeling approval summary was signed off on 03/11/98.

Method validation request was issued on 10/07/98. Northeast Regional Laboratory sent the report (dated 12/03/98), which concluded that Copley's method appears to be suitable for regulatory analysis.

Acceptable EER has not been received as of 08/30/99.

18. **CONCLUSIONS AND RECOMMENDATIONS**:

Approvable (pending acceptable EER)

19. **REVIEWER**: Shing H. Liu, Ph.D. **DATE COMPLETED**: 08/30/99

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chem Rev #5

8/30/99

# Office of Generic Drugs

**Chemistry, Manufacturing and Controls Review**

1. **CHEMIST'S REVIEW NO**: No. 4 **[Nabumetone Tablets]**

2. **ANDA**: 75-179

3. **NAME AND ADDRESS OF APPLICANT**:
   Copley Pharmaceutical, Inc.
   Attention: I. Nudelman, RAC (Director, Regulatory Affairs)
   25 John Road, Canton, MA 02021

4. **LEGAL BASIS for ANDA SUBMISSION**: See CR #1

5. **SUPPLEMENT(s)**: N/A

6. **PROPRIETARY NAME**: N/A

7. **NONPROPRIETARY NAME**: Nabumetone Tablets, 500 mg and 750 mg

8. **SUPPLEMENT(s) PROVIDE(s) FOR**: N/A

9. **AMENDMENTS AND OTHER DATES**:

   Copley:

| | |
|---|---|
| 08/04/97 | Submission of ANDA (received on 08/05/97) |
| 10/02/97 | Amendment (Re: Paragraph IV certification) |
| 10/24/97 | Amendment (addition of 500 mg tablet strength) |
| 03/02/98 | Response to NA (MAJOR) of 01/12/98 (from CR#1) |
| 03/05/98 | Response to Bioequivalence deficiencies |
| 07/16/98 | Bio amendments (two letters with the same date) |
| 07/20/98 | Bio amendment |
| 09/18/98 | Response to NA MINOR of 08/04/98 (from CR#2) |
| 04/22/99 | *Response to NA MINOR of 11/03/98 (from CR#3) |

   FDA:

| | |
|---|---|
| 09/05/97 | Ackowledgment letter |
| 01/12/98 | NA (MAJOR) (based on CR #1, and labeling review) |
| 02/05/98 | Bio deficiency Fax (based on bio review of 01/30/98) |
| 07/27/98 | Bio letter (based on Bio review dated 07/21/98) |
| 08/04/98 | NA (MINOR) (based on CR #2 by S. Liu, Ph.D.) |
| 11/03/98 | NA (MINOR) (based on CR #3 by S. Liu, Ph.D.) |

10. **PHARMACOLOGICAL CATEGORY**: Anti-inflammatory

11. **HOW DISPENSED**: Rx

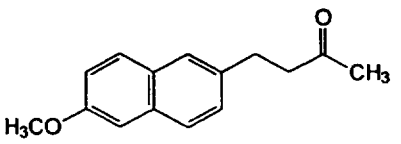
12. **RELATED IND/NDA/DMF(s)**: See CR #2

13. **DOSAGE FORM**: Oral Tablets

14. **Strength**: 500 mg and 750 mg

15. **CHEMICAL NAMES AND STRUCTURE:**

Generic name: Nabumetone
Chemical name: 2-Butanone, 4-(6-methoxy-2 naphthalenyl)-
Formula: $C_{15}H_{16}O$
Molecular weight: 228.29
CAS registry number(s): 42924-53-8
Chemical structure:




16. **RECORDS AND REPORTS:** N/A

17. **COMMENTS:**

Both the bulk drug substance and the drug product do not have USP monographs.

Division of Bioequivalence has completed the review of Copley's bio amendments. DOB's comments was faxed to Copley on 07/27/98.

The of DMF of the drug substance has been reviewed in connection with this amendment (The DMF holder's response to the Agency's DMF deficiency letter was reviewed). The DMF remains deficient. A deficiency letter will be faxed to the DMF holder.

Labeling approval summary was signed off on 03/11/98.

Acceptable EER has not been received. Method validation request was issued on 10/07/98. Northeast Regional Laboratory sent the report dated 12/03/98, which concluded that Copley's method appears to be suitable for regulatory analysis.

18. **CONCLUSIONS AND RECOMMENDATIONS:**

Not approvable (MINOR AMENDMENT, due to DMF deficiency).

19. **REVIEWER:** Shing H. Liu, Ph.D. **DATE COMPLETED:** 04/30/99

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Chem Review 4

4/30/99

# Office of Generic Drugs

**Chemistry, Manufacturing and Controls Review**

1. **CHEMIST'S REVIEW NO**: No. 3

2. **ANDA**: 75-179

3. **NAME AND ADDRESS OF APPLICANT**:
Copley Pharmaceutical, Inc.
Attention: I. Nudelman, RAC (Director, Regulatory Affairs)
25 John Road, Canton, MA 02021

4. **LEGAL BASIS for ANDA SUBMISSION**: See CR #1

5. **SUPPLEMENT(s)**: N/A

6. **PROPRIETARY NAME**: N/A

7. **NONPROPRIETARY NAME**: Nabumetone Tablets, 500 mg and 750 mg

8. **SUPPLEMENT(s) PROVIDE(s) FOR**: N/A

9. **AMENDMENTS AND OTHER DATES**:

Copley:

| | | |
|---|---|---|
| 08/04/97 | | Submission of ANDA (received on 08/05/97) |
| 10/02/97 | | Amendment (Re: Paragraph IV certification) |
| 10/24/97 | | Amendment (addition of 500 mg tablet strength) |
| 03/02/98 | | Response to NA Fax of 01/12/98 (from CR#1) |
| 03/05/98 | | Response to Bioequivalence deficiencies |
| 07/16/98 | | Bio amendments (two letters with the same date) |
| 07/20/98 | | Bio amendment |
| 09/18/98 | * | Response to NA MINOR of 08/04/98 (from CR#2) |

FDA:

| | |
|---|---|
| 09/05/97 | Acknowledgment letter |
| 01/12/98 | NA Fax (based on CR #1, and labeling review) |
| 02/05/98 | Bio deficiency Fax (based on bio review of 01/30/98) |
| 07/27/98 | Bio letter (based on Bio review dated 07/21/98) |

10. **PHARMACOLOGICAL CATEGORY**: Anti-inflammatory

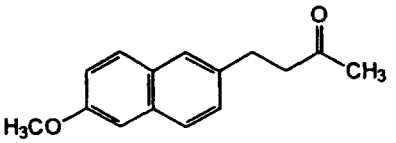
11. **HOW DISPENSED**: Rx

12. **RELATED IND/NDA/DMF(s)**: See CR #2

13. **DOSAGE FORM**: Oral Tablets

14. **Strength**: 500 mg and 750 mg

15. **CHEMICAL NAMES AND STRUCTURE**:
Generic name: Nabumetone
Chemical name: 2-Butanone, 4-(6-methoxy-2 naphthalenyl)-
Formula: $C_{15}H_{16}O$
Molecular weight: 228.29
CAS registry number(s): 42924-53-8
Chemical structure:




16. **RECORDS AND REPORTS**: N/A

17. **COMMENTS**:
Both the bulk drug substance and the drug product do not have USP monographs.

Division of Bioequivalence has completed the review of Copley's bio amendments. DOB's comments was faxed to Copley on 07/27/98.

The of DMF of the drug substance has been reviewed in connection with this amendment (The DMF holder's response to the Agency's DMF deficiency letter was reviewed). The DMF remains deficient. A deficiency letter will be issued to the DMF holder.

Labeling approval summary was signed off on 03/11/98.

Acceptable EER has not been received. Method validation request will be issued, because dissolution method and specifications recommended by DOB have been provided by the applicant.

Copley has provided satisfactory response to the comment we made in the acknowledgment section of the last NA letter.

18. **CONCLUSIONS AND RECOMMENDATIONS**:
Not approvable (MINOR AMENDMENT, due to DMF deficiency).

19. **REVIEWER**: Shing H. Liu, Ph.D.
**DATE COMPLETED**: 10/05/98

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Chem Review

10/5/98

# Office of Generic Drugs

**Chemistry, Manufacturing and Controls Review**

1. **CHEMIST'S REVIEW NO**: No. 2

2. **ANDA**: 75-179

3. **NAME AND ADDRESS OF APPLICANT**:
Copley Pharmaceutical, Inc.
Attention: I. Nudelman, RAC (Director, Regulatory Affairs)
25 John Road, Canton, MA 02021

4. **LEGAL BASIS for ANDA SUBMISSION**:
See CR #1 for details. A copy of letter (dated 11/19/97) from a law firm representing the innovator was filed in the jacket after the last chemistry review. The letter concerns a lawsuit against Copley.

5. **SUPPLEMENT(s)**: N/A

6. **PROPRIETARY NAME**: N/A

7. **NONPROPRIETARY NAME**: Nabumetone Tablets, 500 mg and 750 mg

8. **SUPPLEMENT(s) PROVIDE(s) FOR**: N/A

9. **AMENDMENTS AND OTHER DATES**:

Copley:

| | | |
|---|---|---|
| 08/04/97 | | Submission of ANDA (received on 08/05/97) |
| 10/02/97 | | Amendment (Re: Paragraph IV certification) |
| 10/24/97 | | Amendment (addition of 500 mg tablet strength) |
| 03/02/98 | * | Response to NA Fax of 01/12/98 (from CR#1) |
| 03/05/98 | * | Response to Bioequivalence deficiencies |
| 07/16/98 | * | Bio amendments (two letters with the same date) |
| 07/20/98 | * | Bio amendment |

FDA:

| | |
|---|---|
| 09/05/97 | Acknowledgment letter |
| 01/12/98 | NA Fax (based on CR #1, and labeling review) |
| 02/05/98 | Bio deficiency Fax (based on bio review 0f 01/30/98) |

10. **PHARMACOLOGICAL CATEGORY**: Anti-inflammatory

11. **HOW DISPENSED**: Rx

12. **RELATED IND/NDA/DMF(s)**:
See Item 37 for a complete list of DMFs.

The following deficiency was cited in the last NA letter:

**Deficiency #2**: Response is satisfactory
**Please provide a consolidated list of Drug Master Files (DMFs) that are referenced in the submission. In the original**

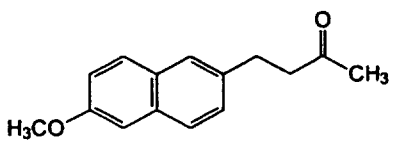
**submission, the list was not included. The DMF list provided in the amendment does not include the bottle used for the 750 mg strength product under DMF No. 4671. There is also an error for Ferro Corporation's DMF number.**

In response, Copley provided a consolidated list. Noted that the holder of drug substance DMF has been changed.

13. **DOSAGE FORM**: Oral Tablets

14. **Strength**: 500 mg and 750 mg

15. **CHEMICAL NAMES AND STRUCTURE**:
Generic name: Nabumetone
Chemical name: 2-Butanone, 4-(6-methoxy-2 naphthalenyl)-
Formula: $C_{15}H_{16}O$
Molecular weight: 228.29
CAS registry number(s): 42924-53-8
Chemical structure:




16. **RECORDS AND REPORTS**: N/A

17. **COMMENTS**:
Both the bulk drug substance and the drug product do not have USP monographs.

Division of Bioequivalence has completed the review of Copley's bio amendments. DOB's comments will be faxed to Copley.

The of DMF of the drug substance has been reviewed in connection with this amendment (The DMF holder's response to the Agency's DMF deficiency letter was reviewed). The DMF remains deficient. A deficiency letter will be issued to the DMF holder. The other major CMC deficiency is the pending dissolution method and specifications (see above).

Labeling review has been completed. There are no more labeling deficiencies.

Acceptable EER has not been received. Mehtod validation will not be issued until Copley has submitted the specifications and

method for dissolution recommended by DOB.

Copley has provided satisfactory response to the comments we made in the acknowledgment section of the last NA letter.

18. **CONCLUSIONS AND RECOMMENDATIONS**:
Not approvable (MINOR AMENDMENT, due to DMF eficiency).

19. **REVIEWER**:
Shing H. Liu, Ph.D.

**DATE COMPLETED**:
07/17/98
Revised 07/31/98 after the bioequivalence review was completed

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chem Rev 2

7/17/98

# Office of Generic Drugs

## Chemistry, Manufacturing and Controls Review

1. **CHEMIST'S REVIEW NO**: No. 1

2. **ANDA**: 75-179

3. **NAME AND ADDRESS OF APPLICANT**:
Copley Pharmaceutical, Inc.
Attention: William E. Brochu, Ph.D.
Canton Commerce Center, 25 John Road
Canton, MA 02021

4. **LEGAL BASIS for ANDA SUBMISSION**:
The US patent #4,420,639 expires December 13, 2002 without any protected exclusivity. Copley intends to challenge the innovator's patent and has filed Paragraph IV Certification.

5. **SUPPLEMENT(s)**: N/A

6. **PROPRIETARY NAME**: N/A

7. **NONPROPRIETARY NAME**: Nabumetone Tablets, 500 mg and 750 mg

8. **SUPPLEMENT(s) PROVIDE(s) FOR**: N/A

9. **AMENDMENTS AND OTHER DATES**:

Copley:

| | |
|---|---|
| 08/04/97 | Submission of ANDA (received on 08/05/97) |
| 10/02/97 | Amendment (Re: Paragraph IV certification) |
| 10/24/97 | Amendment (addition of 500 mg tablet strength) |

FDA:

| | |
|---|---|
| 09/05/97 | Acknowledgment letter |

10. **PHARMACOLOGICAL CATEGORY**: Anti-inflammatory

11. **HOW DISPENSED**: Rx

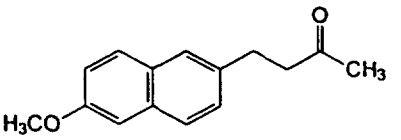
12. **RELATED IND/NDA/DMF(s)**:
See Item 37 for a complete list of DMFs.

**Comment**:
**Copley did not provide a DMF list in their original submission for the 750 mg. But, a list was included in the amendment. Noted that [redacted] was cited for 150 cc bottle only (should be cited for 180 cc bottle also).**

13. **DOSAGE FORM**: Oral Tablets

14. **Strength**: 500 mg and 750 mg

15. **CHEMICAL NAMES AND STRUCTURE**:
Generic name: Nabumetone
Chemical name: 2-Butanone, 4-(6-methoxy-2 naphthalenyl)-
Formula: $C_{15}H_{16}O$
Molecular weight: 228.29
CAS registry number(s): 42924-53-8
Chemical structure:




16. **RECORDS AND REPORTS**: N/A

17. **COMMENTS**:
This ANDA is the first generic application for Nabumetone Tablets. Both the bulk drug substance and the drug product do not have USP monographs.

DMF of the bulk drug substance was reviewed, and was found deficient. There are many CMC deficiencies. The estimated review time of Copley's response to these deficinecies will exceed one hour.

Labeling review has been completed. There are labeling deficiencies. Bioequivalence review is pending. As such, acceptance of the proposed dissolution method and specifications, as well as the proposed expiration dating period is contingent upon the results of the bioequivalence review.

EER should be amended to include all contract laboratories referenced in the submission.

18. **CONCLUSIONS AND RECOMMENDATIONS**:
Not approvable (MAJOR AMENDMENT)

19. **REVIEWER**: Shing H. Liu, Ph.D.

**DATE COMPLETED**: 12/05/97 (revised 12/10/97)

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Alen Rev. 1
12/5/97